REMARKS

I. STATUS OF THE APPLICATION.

Claims 1, 4, 6, 8-16, 19-23, 25-27, 30, 32, 34-38, 41-45, 47 and 48 are presently pending and stand rejected. By way of this response, four (4) claims have been amended. Applicant respectfully submits that no new matter has been added by way of this amendment.

Support for the amendment to claims 1, 25, 27 and 47 can be found at least in paragraphs [0040] and [0049]-[0052] of the application as published (US 2006/0211664).

II. DOUBLE PATENTING REJECTION.

Claims 1, 4, 6, 8-16, 19-23, 25-27, 30, 32, 34-38, 41-45, 47 and 48 stand provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 4-7, 10-16, 18-23, 25-27, 30-33, 35-38, 40-45, and 47-48 of copending U.S. Patent Appl. No. 10/867,435. Applicant will submit a terminal disclaimer once allowable subject matter is indicated.

III. THE REFERENCES COMBINED IN THE OFFICE ACTION DO NOT RENDER ANY OF THE PENDING CLAIMS UNPATENTABLE UNDER 35 U.S.C. § 103(a).

Claims 1, 4, 6, 8-16, 19-23, 25-27, 30, 32, 34-38, 41-45, 47 and 48 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over U.S. Patent No. 5,730,987 ("Omar"), WO 99/24041 ("Mak") and WO 93/25168 ("Heiber") in view of WO 96/27372 ("Allen") and US 6,200,591 ("Hussain"). Applicant respectfully traverses the rejection and respectfully requests that the rejection be withdrawn in light of the arguments set forth below and the present amendments to the claims.

As stated in Applicant's Office Action Response dated December 8, 2009, incorporated by reference herein, the Examiner has failed to establish a *prima facie* case of obviousness. To

establish a *prima facie* case of obviousness, the following basic criteria must be met: (i) the references, alone or as a whole, must disclose each and every limitation of the claimed invention, (ii) there must be a reasonable expectation of success, and (iii) there must be some apparent reason to combine the cited references. M.P.E.P. §§ 2143 and 2141.02

First, Applicant maintains that the combined teachings of the cited references fail to disclose, explicitly or inherently, every limitation of the presently pending claims. In particular, (1) a testosterone gel composition comprising, *inter alia*, isopropyl myristate as the sole penetration enhancer, and (2) the use of a phosphodiesterase inhibitor or a pharmaceutical agent for treating erectile dysfunction in combination with testosterone for improving sexual performance. The Examiner notes "that the claims recite the transitional phrase 'comprising' instead of 'consisting of.' 'Comprising' is considered as open phrase that permits additional components [penetration enhancers] added to the composition." Office Action at 6. Without admitting or conceding in any manner the appropriateness of the rejection, and solely to expedite prosecution of the present application, Applicant has amended claims 1, 25, 27 and 47 to recite a composition "consisting essentially of" or that "consists essentially of" the claimed components and thus the pending claims contemplate a pharmaceutical composition containing isopropyl myristate as the *sole* penetration enhancer.

As M.P.E.P § 2111.03 makes clear, "the transitional phrase 'consisting essentially of' limits the scope of a claim to the specified materials or steps and those that do not materially affect the basic and novel characteristic(s) of the claimed invention." As explained *infra*, the addition of other penetration enhancers would materially affect the basic and novel characteristics, i.e., the pharmacokinetics, of the claimed transdermal testosterone composition.

Thus, by limiting the claims to recite "consisting essentially of," Applicant has effectively excluded the presence of other penetration enhancers from the claimed invention.

Second, Applicant maintains that a person of ordinary skill in the art would have no reasonable expectation that the combination of references suggested in the Office Action would successfully result in the claimed invention. The Examiner asserts that "the motivation to employ isopropyl myristate is present since it is a well-known penetration enhancer and also well compatible with the herein claimed actives." Office Action at 6. The Examiner's argument is not supported in fact. Indeed, the FDA has recognized that different penetration enhancers can unpredictably affect the pharmacokinetics of transdermal testosterone formulations. While the decisions of the FDA are not precedent to the USPTO, it is evidence of the state of art at the time of the invention. In the context of transdermal testosterone gels, the FDA has found that any change in the penetration enhancer would create an unknown risk of testosterone transfer thereby precluding the approval of a generic transdermal testosterone per an Abbreviated New Drug Application, and requiring a full New Drug Application so that any alterations in the transfer to persons in contact with the patient using the testosterone gel can be fully studied and understood. *Auxillium Pharmaceutical, Inc. Citizen's Petition Decision*, at 5, August 26, 2009, Docket No. FDA-2009-P-0123 (See Information Disclosure Statement filed herewith). The FDA recognized what is replete in the literature: that different penetration enhancers may affect skin differently and may cause different degrees of skin irritation and sensitization. *Id.* at 7. Accordingly, based on the combined teachings of the cited references, one of ordinary skill in the art would have no reasonable expectation that isopropyl myristate would be "well compatible with the herein claimed actives" to successfully result in the presently pending claims.

Lastly, Applicant maintains that no apparent reason or motivation exists to combine the references as suggested in the February 22, 2010 Office Action. Each of the cited references specifically emphasize the unique advantages of their disclosed formulations. As such, one of ordinary skill in the art at the time of the invention would have no apparent reason or motivation to venture outside the formulations provided therein and substitute their respective penetration enhancers with isopropyl myristate as the sole penetration enhancer. Specifically, the cited references teach the following advantageous formulations:

- Omar emphasizes the synergistic effect of gingko biloba extract and lyophilized roe and the benefits thereof. *See* Omar, 3:14-19 – 4:27-39.
- Mak discloses a penetration-enhancing system comprising oleic acid as the penetration enhancer, which surprisingly exhibits reduced skin irritation. *See* Mak, page 5, lines 15-30.
- Heiber discloses a transdermal/transmucosal drug delivery system that contains glycerin that acts as a permeation flux moderator and moderates "burst effect," which Heiber describes as "[the delivery system] may deliver a very high dose of the drug initially which then drops or levels off after a period of time to reach acceptable levels" to maintain a relatively uniform dosing profile. *See* Heiber, page 3, lines 16-23 and page 4, lines 21-25.
- Allen teaches a stable, uniform, water-based topical cream containing nitroglycerin for treating a male patient suffering from erectile dysfunction. Notably, Allen teaches that "[t]he results and properties achieved by the present invention are due to the ***judicious selection*** of the ingredients and their relative amounts. (emphasis added)" *See* Allen, page 7, lines 18-26.

- Hussain discloses an intranasal delivery of sildenafil.

The Examiner has failed to provide any reason or motivation that one skilled in the art at the time of the invention would combine the cited references. Indeed, the Examiner asserted only that "[t]he composition of the cited prior art containing testosterone is well-known to be useful for treating erectile dysfunction. Penetration enhancer is known to be useful in enhancing the delivery of testosterone and thus, the efficacy and effectiveness of testosterone for treating ED." Office Action at 5. In light of the above disclosures, it is clear that the Examiner's assertion is without merit. One of ordinary skill in the art would not be motivated to substitute penetration enhancers for fear of losing the advantages of the formulations disclosed in the cited references.

At least for the foregoing reasons, the Examiner has failed to establish a *prima facie* case of obviousness. Thus, in light of the arguments set forth above, and the present amendments to the claims, Applicant respectfully requests withdrawal of the rejection of claims 1, 4, 6, 8-16, 19-23, 25-27, 30, 32, 34-38, 41-45, 47 and 48 under 35 U.S.C. § 103(a).

CONCLUSION

For at least the foregoing reasons, it is respectfully submitted that the amended claims are in condition for allowance. Early and favorable consideration is respectfully requested, and the Examiner is encouraged to contact the undersigned with any questions or to otherwise expedite prosecution. Further, none of Applicant's amendments or cancellations are to be construed as dedicating any such subject matter to the public, and Applicant reserves all rights to pursue any such subject matter in this or a related patent application.

Respectfully submitted,

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